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August 9th 1960

Dr. Joshua Lederberg
Department of Genetics
Stanford University
Medical Center
Palo Alto
California
U.S.A.

Dear Joshua,

Thanks for your letter of July 20th. I appreciate your continued great interest.

Meanwhile Zaffaroni was here and we had a good discussion. I was quite impressed by the activity and drive of the Syntex and I expressed my definite interest in the possible participation of building up the Unit at Palo Alto. Zaffaroni promised to send me further details and definite proposals, as regard conditions of contract, budget, collaborators etc. And no doubt, before making the final decision I would have to contact you, Djerassi and the responsible leaders of the company personally. One thing which worries me is the continuity of such a place. I have been working here for 7 years for WHO and about every year we had to worry whether we would get our budget through and the positions retained. Of course, this might be unique for WHO since they have no laboratories otherwise. Many things remained undone because no long term planning was possible. In fact, to produce decent work one should not have to care about the stability element, just as I have never believed that a poet or painter must necessarily live under strain and famine to produce good work. And quite frankly, Syntex, according to the honest admission of Zaffaroni, has changed hands and affiliations many times in a relatively short time. For a perhaps oldfashioned European this looks disturbing from the distance, for you with the close up view it might mean a sign of juvenile health. But naturally you know the set up much better, and I am convinced I could, and would have to, rely entirely on your judgement and knowledge in this matter.

As mentioned in an earlier note, I have some negotiations going with several universities in Switzerland. In a few weeks I plan to discuss these matters personally there and hope to have then a clearer picture. I suppose the Syntex proposals will have arrived here too by that time. And then there is the possibility to stay here, as chief of the department, in this Institute with unique facilities for immunological work. In that case I would have to become a Danish citizen. So you see, I have quite some problems to decide within the near

future and what I need are facts here and there.

Best wishes,

Yours sincerely,

Ernst Sorkin

P.S. I am quite excited about Szilard's article on Ab-formation, although I do not understand a good part of it. But I wonder what your views are? Somehow I think we have to look upon Ab-formation as a "press-button system", where a seemingly innocent group as sulphanilic acid or a sequence of a few amino acids etc. can trigger off cell differentiation concurrent with Ab-formation. Is it not a fact that the effect of any such determinant group results always in the same generel effect: stem cell ⟶ immature plasma cell ⟶ mature plasma cell? So it seems really conceivable that the only thing which the antigenic group does is taking the "repressor(s)" of Ab-forming enzymes away.* This would be "elective" in your sense, each antibody having a different repressor. This latter statement seems a bit hard, but why not. **

* and other enzymes subsequently follow

The real question is how one could possibly experimentally test this repressor idea. One might postulate that in normal reticular cells there is uncombined repressor. If one could get such a preparation into Ab-forming cells they should be able to interfere with depressed Ab-forming enzymes and synthesis should stop. We did a few crude experiments of this kind, without success, i.e. synthesis as measured by incorporation of C^{14}-amino acids in Ab proceeded undisturbed whether normal or antibody forming tissue extract was added.

Have you any suggestion in this direction, or do you think it's wasted time to do such experiments?

E.S.

** There should then exist an information sequence where complementariness is as follows:

Antigenic determinant	+
Repressor	−
Enzyme	+
Antibody	−

DNA → DNA → Antibody